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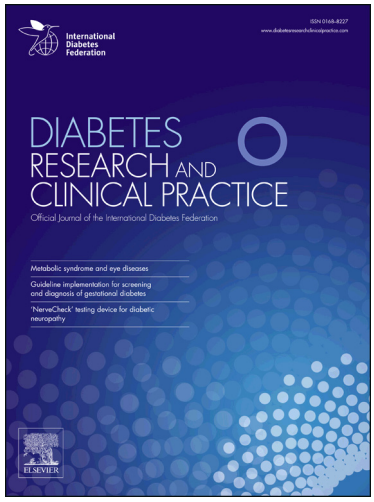

Heparanase-driven Inflammation from the AGEs-stimulated Macrophages Changes the Functions of Glomerular Endothelial Cells

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Heparanase-driven Inflammation from the AGEs-stimulated Macrophages Changes the Functions of Glomerular Endothelial Cells

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Abstract

Aims: Amounts of macrophages were infiltrated in glomeruli in diabetic nephropathy. Heparanase has been thought to be closely related to proteinuria. Our aims were to determine the effect of heparanase on the inflammation in AGEs-stimulated macrophages and its role on the functions of glomerular endothelial cells (GEnCs).

Methods: The expression of inflammation cytokines in macrophages were assayed by q-RT PCR, western, and ELISA. Then western was used to measure the expression of RAGE and key proteins in NF-κB pathway in macrophages. The expression of the adherence molecules and tight junction proteins in GEnCs were assessed by western. The adherence of mononuclear cells to GEnCs were observed by HE staining and transendothelial FITC-BSA were tested for the permeability of GEnCs.

Results: HPA siRNA and heparanase inhibitor sulodexide could attenuate the increasing inflammatory factors (TNF-α and IL-1β) in AGEs-stimulated macrophages. NF-κB inhibitor PDTC could also decrease the augmented inflammation cytokines through inhibiting the activation of the NF-κB pathway induced by AGEs. The phosphorylation of NF-κB signaling pathway could be also attenuated by HPA siRNA and sulodexide, the same to the receptor of AGEs RAGE. When the macrophage-conditioned culture medium were added to the glomerular endothelial cells, we found HPA siRNA and sulodexide groups could decrease the increasing adherence and permeability of GEnCs induced by AGEs.

Conclusions: Heparanase increases the inflammation in AGEs-stimulated macrophages through activating the RAGE-NF-κB pathway. Heparanase driven inflammation from AGEs-stimulated macrophages increases the adherence of GEnCs and augments the permeability of GEnCs.

Key words: Heparanase, advanced glycation end products, inflammatory factor, permeability, glomerular endothelial cell